Insulin resistance following childhood craniopharyngioma may influence neural response to food cues in food reward-related brain regions: a preliminary investigation.

Eleanor C. Hinton¹, Kruthika Narayan², Rebecca L. Elsworth¹, Fiona E. Litherland³, Ninmra Naeem³, Ruth Elson¹, Tashunika Taylor-Miller⁴, Aileen Wilson⁵, Julian P. Hamilton-Shield⁵, Elizabeth C. Crowne⁶

1 Bristol Biomedical Research Centre, 2 Department of Paediatric Endocrinology & Diabetes, Bristol Royal Hospital for Children

This project is funded by the National Institute for Health Research (NIHR) Bristol Biomedical Research Centre at University Hospitals Bristol NHS Foundation Trust and the University of Bristol. The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

¹ NIHR Bristol Biomedical Research Centre Nutrition Theme, University of Bristol
² Bristol Medical School, University of Bristol

BACKGROUND

• Craniopharyngioma is a benign tumour arising in the sellar and suprasellar regions, proximal to the hypothalamic area. Incidence is rare (0.5-2 cases per million per year)⁷.
• Long term sequelae include endocrine dysfunction, visual impairment and hypothalamic obesity⁸, with a negative impact on quality of life⁹.
• Although 50% of craniopharyngioma patients experience hypothalamic obesity – predicted by hypothalamic damage on MRI in some instances⁴ – there is limited research investigating underlying mechanisms, which are poorly understood.
• Hypothalamic damage following craniopharyngioma may have wide-spread effects, e.g.
  ➢ differential neural responses to food cues in the brain⁵,⁶
  ➢ dysfunctional parasympathetic nervous system activity leading to altered glucose metabolism and hypothalamic obesity⁶.
• Evidence in healthy volunteers suggests a link between insulin resistance (IR), neural responses to food and obesity⁶,⁷.

AIM & HYPOTHESIS

Aim: To explore a potential link between IR and neural responses to food and obesity in patients with childhood craniopharyngioma.

Hypothesis: IR in craniopharyngioma may alter neural response to food cues, as measured by fMRI, in several brain regions of interest (ROIs), and thereby contribute to obesity. ROIs: hypothalamus, insula, amygdala, nucleus accumbens, putamen, orbitofrontal cortex, temporal occipital fusiform cortex.

This is part of a larger feasibility study which investigated eating behaviours, energy homeostasis and obesity in patients with childhood craniopharyngioma using various techniques (e.g. oral glucose tolerance test, indirect calorimetry, ad libitum meal, functional MRI).

METHODS

Patients with craniopharyngioma (Cue Reactivity)

n = 11; median age = 14y (range = 10
long term sequelae include endocrine dysfunction, visual impairment and hypothalamic obesity⁸, with a negative impact on quality of life⁹.

Hypothalamic damage following craniopharyngioma may have wide-spread effects, e.g.
• differential neural responses to food cues in the brain⁵,⁶
• dysfunctional parasympathetic nervous system activity leading to altered glucose metabolism and hypothalamic obesity⁶.
• Evidence in healthy volunteers suggests a link between insulin resistance (IR), neural responses to food and obesity⁶,⁷.

AIM & HYPOTHESIS

Aim: To explore a potential link between IR and neural responses to food and obesity in patients with childhood craniopharyngioma.

Hypothesis: IR in craniopharyngioma may alter neural response to food cues, as measured by fMRI, in several brain regions of interest (ROIs), and thereby contribute to obesity. ROIs: hypothalamus, insula, amygdala, nucleus accumbens, putamen, orbitofrontal cortex, temporal occipital fusiform cortex.

This is part of a larger feasibility study which investigated eating behaviours, energy homeostasis and obesity in patients with childhood craniopharyngioma using various techniques (e.g. oral glucose tolerance test, indirect calorimetry, ad libitum meal, functional MRI).

METHODS

• Overnight fast
• Body composition (Tanita)
• Baseline fMRI scan
• Fixed glucose load/kg (OGTT)
• 60 mins
• Post glucose fMRI scan

As this feasibility study was not powered for null hypothesis significance testing, we focused on measure of effect size (r) and correlation coefficients.

INSULIN RESISTANCE AND BODY COMPOSITION

No evidence for a correlation was found between HOMA-IR and body fat % (r=−.25) or BMISDS (r=0.00) (n=9).

INSULIN RESISTANCE AND NEURAL RESPONSES

Relationship between HOMA-IR and neural response to food cues (n=7; Kendall’s tau):

<table>
<thead>
<tr>
<th>HOMA-IR</th>
<th>TOFD</th>
<th>Angiodyala</th>
<th>Hypothalamus</th>
<th>Insula</th>
<th>Nucleus accumbens</th>
<th>Putamen</th>
<th>Baseline</th>
<th>Post-glucose</th>
<th>Crossbars</th>
<th>Post-glucose</th>
<th>Crossbars</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>0.496</td>
<td>-2.328</td>
<td>0.128</td>
<td>-0.143</td>
<td>-0.333</td>
<td>0.465</td>
<td>-0.333</td>
<td>-0.048</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

DISCUSSION

• Preliminary results showed:
  ➢ The expected relationship between insulin resistance and measures of body composition (BMISDS and body fat) was not found.
  ➢ Evidence for a relationship between IR with the BOLD response was found (akin to ¹), both after fasting and after glucose consumption, similar to the hypothalamic response to food cues in people without craniopharyngioma⁹,¹².
  ➢ Results should be considered in the light of differences in brain volume¹⁰, beyond the immediate tumour area, which was related to hypogonadism.

CONCLUSION

These preliminary findings in this small group of craniopharyngioma patients suggest that insulin resistance may influence the response to food cues in brain regions responsible for appetite control. Further investigation of this intriguing link is warranted in larger, multicentre studies.

References: Muller (2014), Gue & Cama (2007), Willjren et al. (2017), Muller et al. (2009), Roth et al. (2010), Roth et al. (2012), Elsworth et al. (2021), Han tentall et al. (2019), Cheke et al. (2017), Winkler et al. (2014), Hinton et al. (2004), Mathusa et al. (1999), Hinton et al. (2001).

Trial registered with ISRCTN (archiv.is/ISRCTN86001617)

This project is funded by the National Institute for Health Research (NIHR) Bristol Biomedical Research Centre at University Hospitals Bristol NHS Foundation Trust and the University of Bristol. The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.